# Non-viral reprogramming of the endogenous TCRα locus to direct stem memory T cells against shared neoantigens in malignant gliomas

## Grant Award Details

Non-viral reprogramming of the endogenous TCRα locus to direct stem memory T cells against shared neoantigens in malignant gliomas

**Grant Type:** Quest - Discovery Stage Research Projects

**Grant Number:** DISC2-11036

**Investigator:**

| | |
|---|---|
| **Name:** | Hideho Okada |
| **Institution:** | University of California, San Francisco |
| **Type:** | PI |

**Disease Focus:** Brain Cancer, Cancer, Solid Tumors

**Human Stem Cell Use:** Adult Stem Cell

**Award Value:** $900,000

**Status:** Pre-Active

## Grant Application Details

**Application Title:** Non-viral reprogramming of the endogenous TCRα locus to direct stem memory T cells against shared neoantigens in malignant gliomas

**Public Abstract:**

**Research Objective**

We will develop a non-viral gene editing technology to replace the endogenous TCRα locus of stem memory T cells with transgene TCRs that are specific to brain cancer neoantigens.

**Impact**

Gliomas are lethal tumors often affecting children and young adults. Therapy using Tscm directed to attack truncal neoantigens in these tumors may provide long-lasting protective immunity.

**Major Proposed Activities**

- Establish and optimize the TCR replacement in CD8+ or CD4+ Tscm with H3.3K27M-specific or IDH1(R132H)-specific TCRs, respectively.
- In vitro evaluation of TCR-replaced Tscm for their functional avidity in comparison to Tscm engineered with the conventional retroviral TCR vector and CRISPR-knock out of endogenous (e)TCR.
- In vivo evaluation of TCR-replaced Tscm cells for anti-glioma effects in comparison with Tscm engineered with the conventional retroviral TCR vector and CRISPR-knock out of eTCR.

**Statement of Benefit to California:**

In children, brain tumors are the leading cause of cancer-related mortality and morbidity. Furthermore, IDH1-mutant gliomas tend to occur in young adults. Our institution is one of the largest brain tumor centers in the world, developing a number of innovative clinical trials and treating patients primarily from CA. The proposed study will establish a strong basis to develop a novel, safe and effective stem memory T cell therapy for patients with malignant brain tumors, including ones in CA.

---